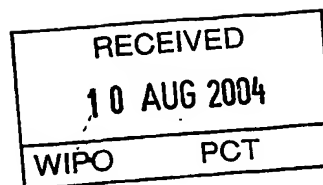


PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference PCA20424/HMY	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/KR2002/000588	International filing date (day/month/year) 03 APRIL 2002 (03.04.2002)	Priority date (day/month/year)
International Patent Classification (IPC) or national classification and IPC IPC7 C07H 17/08		
Applicant HANMI PHARM. CO., LTD. et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 3 sheets, including this cover sheet.
☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
 These annexes consist of a total of _____ sheets.
3. This report contains indications relating to the following items:
 - I ☒ Basis of the report
 - II ☐ Priority
 - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☐ Certain observations on the international application

Date of submission of the demand 21 OCTOBER 2003 (21.10.2003)	Date of completion of this report 28 JULY 2004 (28.07.2004)
Name and mailing address of the IPEA/KR Korean Intellectual Property Office 920 Dunsan-dong, Seo-gu, Daejeon 302-701, Republic of Korea Facsimile No. 82-42-472-7140	Authorized officer CHO, Myung Sun Telephone No. 82-42-481-5594

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/KR2002/000588

I. Basis of the report

1. With regard to the elements of the international application:*

- ☒ the international application as originally filed
- ☐ the description:
 pages _____, as originally filed
 pages _____, filed with the demand
 pages _____, filed with the letter of _____
- ☐ the claims:
 pages _____, as originally filed
 pages _____, as amended (together with any statement) under Article 19
 pages _____, filed with the demand
 pages _____, filed with the letter of _____
- ☐ the drawings:
 pages _____, as originally filed
 pages _____, filed with the demand
 pages _____, filed with the letter of _____
- ☐ the sequence listing part of the description:
 pages _____, as originally filed
 pages _____, filed with the demand
 pages _____, filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language English which is

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☒ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheet _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed." and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item I and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION

International application No.

PCT/KR2002/000588

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-11	YES
	Claims	none	NO
Inventive step (IS)	Claims	1-11	YES
	Claims	none	NO
Industrial applicability (IA)	Claims	1-11	YES
	Claims	none	NO

2. Citations and explanations (Rule 70.7)

(1) The present application claims a method of preparing azithromycin of formula (I), a crystalline hydrate 9-deoxo-9a-aza-9a-homoerythromycin of formula II and the method of preparing the formula II.

(2) Document D1 (EP 879,823 A) has been considered as the most closest prior art out of the documents listed in the International Search Report. Both D1 and claims 1-6 in the present application are disclosing the method of preparing azithromycin of formula (I), consisting of the reduction process of the imino ether of formula III using sodium borohydride to yield the formula II (step [a]) and N-methylation process of the formula II to produce the final product of formula I(step [b]).

(3) The difference lies in that the process of step [b] in D1 is continued in the same reaction mixture as in the process of step [a] without isolating procedure of formula II as crystalline hydrate form and it requires the reduction catalyst such as rhodium-on-carbon, while the step [a] in claims 1-6 includes further steps to provide the crystalline form of the compound II and the step [b] is conducted with a formic acid and a soluble formaldehyde in organic solvent without adding a catalyst.

Thus, claims 1-6 meet the criteria for novelty, inventive step and industrial applicability set out in Article 33(2)-(4) PCT.

(4) None of the documents in the International Search Report including D1 is disclosing either the crystalline hydrate form of formula II specified in claims 7-8 or specific reaction conditions to prepare the same as described in claims 9-11.

Therefore, Claims 7-11 are also regarded to meet the requirements of Article 33 (2)-(4) PCT.